RECEIVED
CENTRAL FAX CENTER

APR 1 8 2007

In the Specification

Please substitute the following paragraph beginning on page 15, line 28, through to page 16, line 14:

The functionally-equivalent polypeptides of the first aspect of the invention may be polypeptides that are homologous to the INSP037 polypeptides. Two polypeptides are said to be "homologous", as the term is used herein, if the sequence of one of the polypeptides has a high enough degree of identity or similarity to the sequence of the other polypeptide. "Identity" indicates that at any particular position in the aligned sequences, the amino acid residue is identical between the sequences. "Similarity" indicates that, at any particular position in the aligned sequences, the amino acid residue is of a similar type between the sequences. Degrees of identity and similarity can be readily calculated (Computational Molecular Biology, Lesk, A.M., ed., Oxford University Press, New York, 1988; Biocomputing. Informatics and Genome Projects, Smith, D.W., ed., Academic Press, New York, 1993; Computer Analysis of Sequence Data, Part 1, Griffin, A.M., and Griffin, H.G., eds., Humana Press, New Jersey, 1994; Sequence Analysis in Molecular Biology, von Heinje, G., Academic Press, 1987; and Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M Stockton Press, New York, 1991). Preferably, percentage identity, as referred to herein, is as determined using BLAST version 2.1.3 using the default parameters specified by the NCBI (the National Center for Biotechnology Information; ~~http://www.ncbi.nlm.nih.gov/~~ See Worldwide Website: ncbi.nlm.nih.gov/) [Blosum 62 matrix; gap open penalty=11 and gap extension penalty=1].

Please substitute the following paragraph beginning on page 43, line 26:

The technology referred to as jet injection (see, for example, ~~www.powderject.com~~ see Worldwide Website: powderject.com) may also be useful in the formulation of vaccine compositions.

Please substitute the following paragraph beginning on page 52, line 1:

Human cDNA libraries (in bacteriophage lambda (λ) vectors) were purchased from Stratagene or Clontech or prepared at the Serono Pharmaceutical Research Institute in λ ZAP or λ GT10 vectors according to the manufacturer's protocol (Stratagene). Bacteriophage λ DNA was prepared from small scale cultures of infected *E.coli* host strain using the ~~Wizard~~ WIZARD Lambda Preps DNA purification system according to the manufacturer's instructions (Promega, Corporation, Madison WI.) The list of libraries and host strains used is shown in Table 1.

Please substitute the following paragraph beginning on page 54, line 13:

The amplification products were visualized on 0.8 % agarose gels in 1 X TAE buffer (Life Technologies) and PCR products migrating at the predicted molecular mass were purified from the gel using the ~~Wizard~~ WIZARD PCR Preps DNA Purification System (Promega). PCR products eluted in 50 µl of sterile water were either sub-cloned directly or stored at –20 ^{0}C.

Please substitute the following paragraph beginning on page 55, line 20:

Miniprep plasmid DNA was prepared from 5 ml cultures using a ~~Qiaprep~~ QIAPREP Turbo 9600 robotic system (Qiagen) or ~~Wizard~~ WIZARD Plus SV Minipreps kit (Promega cat. no. 1460) according to the manufacturer's instructions. Plasmid DNA was eluted in 100 µl of sterile water. The DNA concentration was measured using an Eppendorf BO photometer. Plasmid DNA (200-500 ng) was subjected to DNA sequencing with T7 primer and SP6 primer using the ~~BigDyeTerminator~~ BIGDYE TERMINATOR system (Applied Biosystems cat. no. 4390246) according to the manufacturer's instructions. Sequencing reactions were purified using Dye-Ex columns (Qiagen) or ~~Montage~~ MONTAGE SEQ 96 cleanup plates (Millipore cat. no. LSKS09624) then analyzed on an Applied Biosystems 3700 sequencer.

Please substitute the following paragraph beginning on page 56, line 3:

A pCRII-TOPO clone containing the full coding sequence (ORF) of IPAAA44548 identified by DNA sequencing (Figure 5) was then used to subclone the insert into the mammalian cell expression vector pEAK12d (Figure 6) using the ~~Gateway~~™ GATEWAY cloning methodology (Invitrogen). The cloned sequence contains a single nucleotide substitution A134G (Figure 4).

Please substitute the following paragraph beginning on page 56, line 10:

The first stage of the ~~Gateway~~ GATEWAY cloning process involves a two step PCR reaction which generates the ORF of IPAAA44548 flanked at the 5' end by an attB1 recombination site and Kozak sequence, and flanked at the 3' end by a sequence encoding an in frame 6 histidine (6HIS) tag, a stop codon and the attB2 recombination site (~~Gateway~~ GATEWAY compatible cDNA). The first PCR reaction (in a final volume of 50 µl) contains: 25 ng of pCR II TOPO-IPAAA44548 (plasmid 13124 and Figure 5), 2 µl dNTPs (5mM), 5µl of 10X Pfx polymerase buffer, 0.5 µl each of gene specific primer (100 µM) (EX1 forward and EX1 reverse) and 0.5 µl Platinum Pfx DNA polymerase (Invitrogen). The PCR reaction was performed using an initial denaturing step of 95^{0}C for 2 min, followed by 12 cycles of 94 ^{0}C, 15 sec and 68^{0}C for 30 sec. PCR products were purified directly from the reaction mixture using the ~~Wizard~~ WIZARD PCR prep DNA purification system (Promega) according to the manufacturer's instructions. The second PCR reaction (in a final volume of 50 µl) contained 10 µl purified PCR product, 2 µl dNTPs (5 mM), 5 µl of 10X Pfx polymerase buffer, 0.5 µl of each ~~Gateway~~ GATEWAY conversion primer (100 µM) (GCP forward and GCP reverse) and 0.5 µl of Platinum Pfx DNA polymerase. The conditions for the 2nd PCR reaction were: 95 ^{0}C for 1 min; 4 cycles of 94 ^{0}C, 15 sec; 45 ^{0}C, 30 sec and 68 ^{0}C for 3.5 min; 25 cycles of 94 ^{0}C, 15 sec; 55 ^{0}C , 30 sec and 68 ^{0}C, 3.5 min. PCR products were purified as described above.

Please substitute the following paragraphs beginning on page 57, line 5:

The second stage of the ~~Gateway~~ GATEWAY cloning process involves subcloning of the ~~Gateway~~ GATEWAY modified PCR product into the ~~Gateway~~ GATEWAY entry vector pDONR201 (Invitrogen, Figure 7) as follows: 5 µl of purified PCR product is incubated with 1.5 µl pDONR201 vector (0.1 µg/µl), 2 µl BP buffer and 1.5 µl of BP clonase enzyme mix (Invitrogen) at RT for 1 h. The reaction was stopped by addition of proteinase K (2 µg) and incubated at 37^{0}C for a further 10 min. An aliquot of this reaction (2 µl) was transformed into *E. coli* DH10B cells by electroporation using a Biorad Gene Pulser. Transformants were plated on LB-kanamycin plates. Plasmid mini-prep DNA was prepared from 1-4 of the resultant colonies using ~~Wizard~~ WIZARD Plus SV Minipreps kit (Promega), and 1.5 µl of the plasmid eluate was then used in a recombination reaction containing 1.5 µl pEAK12d vector (Figure 6) (0.1 µg / µl), 2 µl LR buffer and 1.5 µl of LR clonase (Invitrogen) in a final volume of 10 µl. The mixture was incubated at RT for 1 h, stopped by addition of proteinase K (2 µg) and incubated at 37^{0}C for a further 10 min. An aliquot of this reaction (1 µl) was used to transform *E. coli* DH10B cells by electroporation.

Clones containing the correct insert were identified by performing colony PCR as described above except that pEAK12d primers (pEAK12d F and pEAK12d R) were used for the PCR. Plasmid mini prep DNA was isolated from clones containing the correct insert using a ~~Qiaprep~~ QUIPREP Turbo 9600 robotic system (Qiagen) or manually using a ~~Wizard~~ WIZARD Plus SV minipreps kit (Promega) and sequence verified using the pEAK12d F and pEAK12d R primers.

Please substitute the following paragraphs beginning on page 58, beginning at line 2:

The vector pEAK12d is a ~~Gateway~~ GATEWAY Cloning System compatible version of the mammalian cell expression vector pEAK12 (purchased from Edge Biosystems) in which the cDNA of interest is expressed under the control of the human EF1α promoter. pEAK12d was generated as described below:

pEAK12 was digested with restriction enzymes HindIII and NotI, made blunt ended with Klenow (New England Biolabs) and dephosphorylated using calf-intestinal alkaline phosphatase

(Roche). After dephosphorylation, the vector was ligated to the blunt ended ~~Gateway~~ GATEWAY reading frame cassette C (~~Gateway~~ GATEWAY vector conversion system, Invitrogen cat no. 11828-019) which contains AttR recombination sites flanking the ccdB gene and chloramphenicol resistance, and transformed into *E.coli* DB3.1 cells (which allow propagation of vectors containing the ccdB gene). Mini prep DNA was isolated from several of the resultant colonies using a ~~Wizard~~ WIZARD Plus SV Minipreps kit (Promega) and digested with AseI / EcoRI to identify clones yielding a 670 bp fragment, indicating that the cassette had been inserted in the correct orientation. The resultant plasmid was called pEAK12d (Figure 6).

Please substitute the following paragraph beginning on page 58, line 19:

~~Gateway~~ GATEWAY compatible SD-IPAAA44548 ORF containing an in frame 3' 6HIS tag coding sequence and a 5' upstream Shine Dalgarno sequence was subcloned into pDONR201 using BP clonase. The resultant plasmid was then used in a recombination reaction with the *E.coli* expression vector pDEST14 (purchased from Invitrogen, Figure 9) using LR clonase as described above. The resultant expression plasmid (pDEST14-IPAAA44548-6HIS) (Figure 10, plasmid ID 12896) was sequence verified as described above. For expression in *E.coli*, CsCl purified maxi-prep DNA was re-transformed into *E.coli* host strain BL21. The expression of the inserted cDNA is under the control of a T7 promoter.

Please substitute the following paragraph beginning on page 69, line 24:

His or StrepII tagged hIL-6 or IPAAA44548 genes were cloned in the ~~Gateway~~ GATEWAY compatible pDEST12.2 containing the CMV promoter.

Please substitute the following paragraph beginning on page 70, beginning at line 15:

IL-2, IL-5, IL-4, ~~TNFα and IFNβ~~ TNF α and IFN γ cytokine levels were measured using the TH1/TH2 CBA assay (BD 551287). ASpartate AminoTransferase (ASAT), ALanine Amino Transferase ALAT and urea blood parameters were determined using the COBAS instrument (Hitachi).